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Palladium Catalysis

Visual Observation of Redistribution and Dissolution of Palladium during the Suzuki–Miyaura Reaction**

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The use of Pd catalysts in cross-coupling reactions has revolutionized the way organic molecules are made.[1,2] Suzuki–Miyaura, Mizoroki–Heck, Kumada–Corriu, Stille, and Negishi couplings are but a few of the named reactions that provide versatile methods for the construction of organic frameworks. Although advances have been made in the use of alternative metals such as nickel or iron in cross-coupling reactions, palladium remains by far the catalyst of choice for these important reactions.

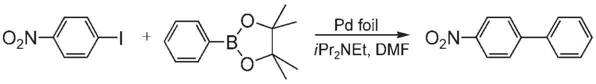
With efficient ways of manufacturing molecules in hand, the main difficulty then becomes removing the catalyst at the completion of the reaction.[3,4] The strict controls regulatory agencies place on the levels of heavy metals in pharmaceutical and related products makes removal of metal catalysts after a reaction an even more serious issue in the pharmaceutical industry.

An obvious approach to solving this problem is to use heterogeneous catalysts which should be removable by filtration. However, the groundbreaking studies of Arai and Kohler showed independently that even traditional heterogeneous catalysts such as Pd/C act by releasing small amounts of soluble Pd, which then redeposit at the completion of the reaction.[5,6] Since this re-deposition removes Pd from solution, understanding how this takes place is critical to developing effective catalysts that are removed after reaction.

With this in mind, we embarked on a study of the Suzuki–Miyaura reaction using Pd foil as the catalyst, to permit the direct visualization of the changes that take place on the metal surface as a result of the Suzuki–Miyaura reaction, including the re-deposition phenomenon. In addition to bulk studies with Pd foil, we have employed a specially designed reactor that allows us to heat only a small portion of the surface to a temperature where reaction can take place, while exposing the entire surface of the foil to the reaction mixture. Using this technique, we demonstrate that both the Suzuki–Miyaura reaction itself and treatment with the aryl iodide alone cause changes in surface chemistry and morphology only where the temperature is sufficient to cause the coupling reaction to take place. In addition, we found that re-deposition of Pd occurs preferentially on the periphery of the reactive zone in cases when only a small portion of the surface is heated.

As the catalyst, we employed 250 μm thick Pd foil.[7–11] Its surface was examined by scanning electron microscopy (SEM), optical microscopy, and X-ray photoelectron spectroscopy (XPS) prior to reaction. The foil is characterized by a relatively smooth, pit-free surface that has ridges spaced at non-periodic distances presumably as a result of the rolling process used to generate the foil. Rather than anneal the foil, we employed these surface features as a frame of reference during the various treatments.

For the Suzuki–Miyaura reaction, we employed the pinacol ester of phenyl boronic acid, and *p*-nitrophenyl iodide. An electron-deficient aryl iodide was chosen to facilitate the coupling reaction. The reaction was first carried out with the entire piece of Pd foil immersed in DMF at 100 °C in a conventional reactor, without stirring, to prevent damage to the Pd surface.



(1)

Figure 1 A shows the Pd foil after treatment with DMF/water at 100 °C,[12] which results in no visible change in the surface morphology. However under the reaction conditions, which gave the desired product in 45 % yield, considerable pitting of the surface of the Pd was observed (Figure 1 B). Exposure to the aryl iodide alone also led to considerable

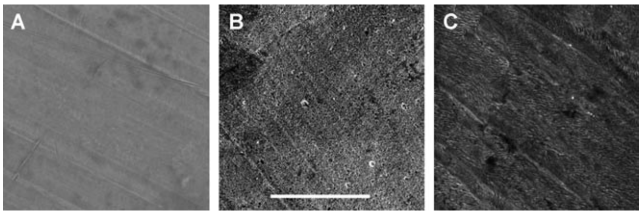


Figure 1. A) Pd surface after exposure to DMF/H_2O at 100 °C for 24 h; B) Pd surface upon completion of successful Suzuki–Miyaura reaction; C) Pd surface after exposure to the aryl iodide in DMF/H_2O at 100 °C for 24 h. Scale bar 20 μm.

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restructuring of the Pd surface (Figure 1C), consistent with the commonly held view that it is the oxidative addition of the aryl iodide that is responsible for removing Pd from the surface in much the same way as magnesium metal is dissolved upon formation of a Grignard reagent.[13–15] Consistent with this, we observed about 100 ppb of Pd in solution by ICPMS after the coupling reaction and after treatment with aryl iodide.

Analysis of the surfaces of the different samples using XPS was carried out to determine what if any chemical changes accompanied the obvious morphological changes observed in the Pd foil, and to rule out simple contamination of the surface with reactants or products. In Figure 2, the XPS spectra (Pd 3d$_{5/2}$, N 1s, and I 3d$_{3/2,5/2}$) obtained for variously reacted Pd foils are collected in addition to that for PdI$_2$.[16]

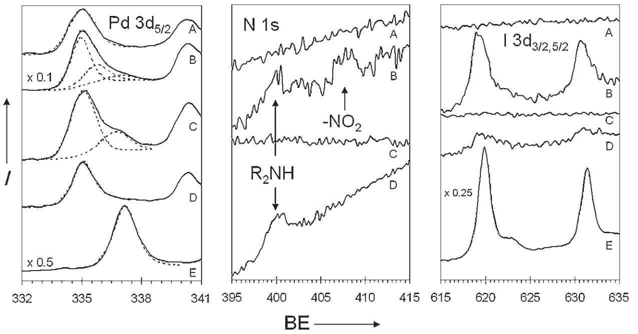

Figure 2. X-ray photoelectron spectra: A) Pd foil washed with DMF; B) Pd foil after the Suzuki–Miyaura coupling reaction; C) sample B after prolonged washing with DMF; D) Pd foil exposed to a solution of *p*-iodonitrobenzene in DMF, E) PdI$_2$.

Sample A, which is Pd foil that has been exposed to DMF, displays a signal in the Pd 3d$_{5/2}$ region at a binding energy of 335.0 eV.[17] Based on literature data, this peak is reasonably assigned to bulk Pd metal.[18–20] As expected, no signal was observed in the I 3d$_{5/2,3/2}$ spectra.[21] Following initiation of the Suzuki coupling reaction on the Pd foil surface, substantial changes in the Pd 3d$_{5/2}$ region of the spectrum can be seen (see sample B). First, the intensity of the spectra is greater than in the case of the starting Pd foil. This is likely due to the increase in surface area that accompanies the observed pitting of the surface (Figure 1B).

Three peaks appear in the Pd 3d$_{5/2}$ region at binding energies of 334.8, 335.7, and 336.8 eV.[22] The first peak is attributed to bulk metallic Pd, and the signal at 336.8 eV is consistent with either Pd oxide or PdI$_2$.[23] After more vigorous washing, the peak at 336.8 eV remains, but no iodine is present (sample C, left). Thus, this peak is likely attributable to Pd oxide.[19,24]

The peak at 335.7 eV, which is removed by extensive washing, appears to be unique to sample B, and contains Pd, N, and I. The spectrum of PdI$_2$ (sample E) has a signal at 337.7, 2 eV higher than the unknown signal. Another possibility is that this signal is attributable to the oxidative addition product from the reaction between Pd and the aryl iodide.

Although iodine is present, assignment of the unknown signal based on the I 3d$_{5/2}$ spectra alone is difficult.[25] The N 1s region of sample C shows one signal attributable to an amine-like environment (likely trace quantities of Hünig's base) and one in the correct range for a nitro group. XPS data indicate that the NO$_2$/I area ratio is (1.6 ± 0.4):1, which is close to the 1:1 value that would be expected for the oxidative addition product. Although contamination of the surface with a trace of unreacted aryl iodide cannot be ruled out, the observation of these signals in addition to a new signal in the Pd spectra is suggestive of a species resulting from oxidative addition into the C(aryl)−I bond.

This type of species has been postulated independently by Reetz and Westermann[13] and Trzeciak et al.[24,26] in studies of Pd nanoparticles in solution and on support. Although a separate signal for the proposed oxidatively added complex ($[Pd(Ph)_xBr_{4-x}]^{2-}$) was not observed definitively in the Pd 3d$_{5/2}$ spectra, Trzeciak et al. suggested that the increased breadth of the signal observed at 336.9 eV may be attributed to this oxidative addition product. The signal we observe at 335.7 eV would also be consistent with Pd^{II}, since a lower binding energy would arise from stabilization of the core hole by extra-atomic relaxation of the polarizable iodo and aryl fragments.

Interestingly, treatment with the aryl iodide alone (sample D) showed no changes in the Pd 3d$_{5/2}$ or N 1s spectra. However, the I 3d$_{5/2,3/2}$ regions of the XP spectrum do show weak signals similar to those observed in sample B. The small size of these signals may be attributed to removal by washing with DMF. The low inherent intensity of N 1s spectra and the significant width of the Pd^0 peak make the observation of small quantities of this species difficult.

Confident that the observed changes in surface structure are not due to adsorption of organic impurities but rather correspond to changes in the surface of the metal, we carried out the same reaction in a cell that permitted us to heat only a small portion of the foil to a temperature at which coupling will take place, while exposing the entire surface to the reaction conditions.

Pd foil was employed as the base of the reactor, onto which a 10 mm diameter Teflon cylinder was attached. Heat was applied to the back of the foil using a metal tip about 1 mm in diameter. A heat sink was attached to the foil to establish a well-defined temperature profile.

The actual temperature profile was examined from the top with an infrared thermal imaging camera.[27] With the heat sink set at 37 °C, we were able to determine that the area of the foil that reached temperatures greater than 60 °C was no more than 3 mm in diameter, and temperatures greater than 100 °C are limited to 1 mm diameter (Figure 3). The bulk temperature in the reaction solvent never increased above ambient as expected from the much higher thermal conductivity of Pd metal compared to the aqueous solution.

We then proceeded to carry out the Suzuki–Miyaura reaction under the same conditions employed in the "bulk" reactor, using the microreactor described above. Although the reaction was considerably slower (ca. 15 % yield after 4 days), coupled product was observed in solution. The decrease in the yield is likely due to the smaller surface

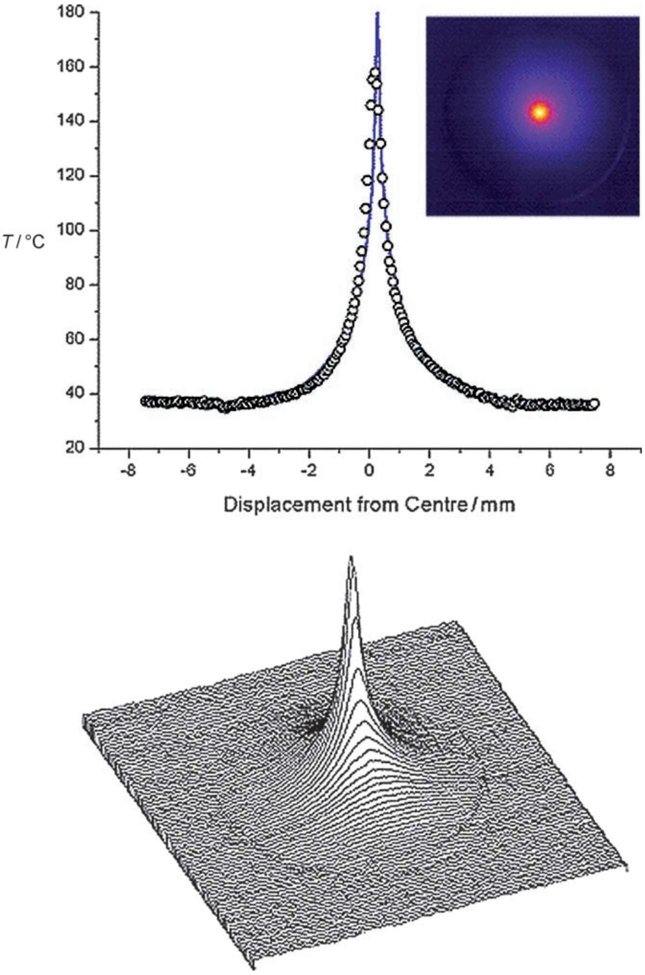

Figure 3. Image of the Pd foil (250 μm) recorded with an IR camera (FLIR ThermaCAM SC1000). The tip of a soldering iron heated to 400 °C was held approximately at the center of the foil underneath the reactor. To record the heat distribution, the Pd foil was coated with soot to decrease reflectance, while mounted on a heat sink held at 37 °C.

area that is heated ($0.8\,mm^2$), and therefore the smaller volume of reaction.

Local heating of the Pd foil in the absence of reactants led to no change in the surface morphology; however, in the presence of the reactants, we observed pitting of the Pd foil only in the area roughly defined by the high-temperature probe. Figure 4 A shows the area of the foil that is outside the heated zone where reaction takes place. It is indistinguishable from the foil treated with only DMF. However, the area contained within the heated zone (Figure 4 C) is dramatically different. The surface exposed to the reactants and heated to an appropriate temperature shows considerable pitting. Figure 4 B shows a region that is at the boundary of the heated and non-heated zones. As previously observed, the aryl iodide also led to significant changes in the surface morphology but other reagents did not.

One significant difference between this experiment and those conducted by heating the entire surface of the Pd foil is the inhomogeneity of the Pd re-deposition. In the case of the point-heated surface, some of the areas immediately beside the heated zone are characterized by significant amounts of what appears to be re-deposited Pd (Figure 5). This is consistent with the re-deposition of Pd occurring in the cool areas of the Pd surface, not far from the heated zone.

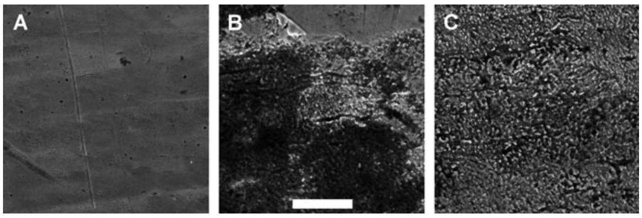

Figure 4. SEM images of the surface of the Pd foil after treatment with spot heater. A) Pd surface outside the heated zone but still exposed to the reactants; B) the transition between heated and not-heated areas of the Pd surface and resultant pitting of the surface; C) Pd surface inside the heated zone where reaction takes place. Scale bar 20 μm.

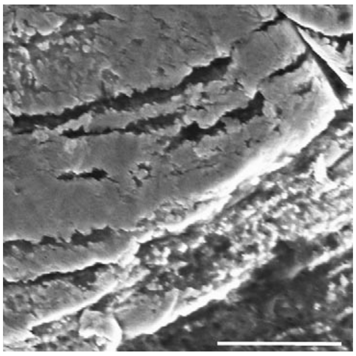

Figure 5. SEM image of the Pd foil in spot-heated experiment showing a section adjacent to the heated area where significant Pd re-deposition has taken place. Scale bar 5 μm.

This leads to the conclusions that 1) the mobility of the Pd is not sufficiently large under these conditions to cover the entire surface and that 2) deposition appears to take place preferentially on the cooler parts of the surface. This latter point is important in terms of the results obtained by Arai and Kohler,[5,6] who showed that deposition of Pd occurs upon cooling of the surface of supported catalysts. It is for this reason that during the commonly employed "hot-filtration-test" for heterogeneity, reactions must be filtered while still hot to prevent deposition of solubilized Pd. To the best of our knowledge, this is the first time the re-deposition phenomenon has been visually observed.

In conclusion, the redistribution of Pd during the Suzuki–Miyaura reaction was observed visually by SEM examination of the surface of Pd foil used as a catalyst for this important reaction. By designing a reactor with which it is possible to heat only a small area of the surface to reactive temperatures, we have been able to demonstrate that pitting of the surface takes place only in reactive zones. Furthermore, re-deposition of Pd appears to take place at the cool edges of these zones rather than uniformly across the surface. XPS examination of the surfaces of these Pd samples demonstrates that the change in surface morphology is not a result of deposition of by-products and furthermore that new Pd species are formed as a result of the reaction. Treatment with aryl iodide also results in pitting of the surface. These results show that at least with Pd foil, reaction likely occurs by dissolution of Pd and re-deposition, both of which are thermally controlled.

Experimental Section

General procedure for the Suzuki–Miyaura coupling reaction: *p*-Nitrophenyl iodide (62 mg, 0.25 mmol) (Aldrich), *N*,*N*-diisopropylethylamine (64 mg, 0.50 mmol), PhBpin (pinacol ester of phenyl boronic acid, 75 mg, 0.375 mmol) were weighed into the reaction vesicle and dry DMF (2.5 mL), degassed by bubbling argon, and distilled H_2O (0.125 mL) were added by syringe. The solution was heated with the palladium foil (Aldrich) without stirring and the reaction progress was monitored by GC-FID.

Bulk palladium foil samples A, B, and D were extracted from the reaction vessel and washed with DMF at 80 °C overnight. After this, the samples were air-dried at room temperature for 24 h. Sample C (Figure 2) was prepared from sample B after it was re-washed with DMF at 80 °C for 8 h, refluxed in THF for 8 h, and then rinsed with EtOAc and CH_2Cl_2.

Samples of palladium foil (shown in Figure 4 and 5) that were exposed to the tip of a soldering iron were washed with DMF at 80 °C for 4 h to remove any organic material, prior to examination of the surface.

XPS measurements were performed by using a Thermo Instruments Microlab 310F surface analysis system (Hastings, UK) under ultrahigh vacuum conditions with a $\mathrm{Mg}_{\mathrm{K}\alpha}$ radiation source at 1253.6 eV. Scans were acquired at fixed analyzer transmission (FAT) mode at a pass energy of 20 eV. All spectra were calibrated to the C 1s line at a binding energy of 284.5 eV. Spectra were background-subtracted using a Shirley fit algorithm and using a Powell peak-fitting algorithm provided in the spectrometer software.[28] Peak areas from different samples were normalized by using the ratio of the background signal 5 eV beyond the Fermi level cut off from the valence band spectra to account for small variations in X-ray source intensity between analyses. XP spectra of PdI_2 (Aldrich 7790387) were obtained by spreading the powdered Pd salt onto a piece of double-sided Cu tape (SPI Supplies Toronto, Ontario), which was then mounted onto the sample holder and transferred through an air lock into the spectrometer.

SEM images were recorded by mounting the palladium foil samples on pins, no conductive coating was required for these samples. A JEOL JSM-840 scanning electron microscope was used to investigate the surfaces.

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[1] *Handbook of Organopalladium Chemistry for Organic Synthesis* (Eds.: E.-I. Negishi, A. de Meijere), Wiley-VCH, Weinheim, **2002**.

[2] *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**.

[3] K. Königsberger, G.-P. Chen, R. R. Wu, M. J. Girgis, K. Prasad, O. Repic, T. J. Blacklock, *Org. Process Res. Dev.* **2003**, *7*, 733.

[4] C. E. Garrett, K. Prasad, *Adv. Synth. Catal.* **2004**, *346*, 889.

[5] K. Kohler, W. Kleist, S. S. Prockl, *Inorg. Chem.* **2007**, *46*, 1876.

[6] F. Y. Zhao, M. Shirai, Y. Ikushima, M. Arai, *J. Mol. Catal. A* **2002**, *180*, 211.

[7] To the best of our knowledge, Pd foil has not been employed in coupling reactions, although it has been used in oxidation and reduction chemistry (see references [8–11]).

[8] D. Teschner, A. Pestryakov, E. Kleimenov, M. Havecker, H. Bluhm, H. Sauer, A. Knop-Gericke, R. Schlögl, *J. Catal.* **2005**, *230*, 195.

[9] C. Descorme, P. W. Jacobs, G. A. Somorjai, *J. Catal.* **1998**, *178*, 668.

[10] R. S. Monteiro, D. Zemlyanov, J. M. Storey, F. H. Ribeiro, *J. Catal.* **2001**, *199*, 291.

[11] E. H. Voogt, A. J. M. Mens, O. L. J. Gijzeman, J. W. Geus, *Surf. Sci.* **1997**, *373*, 210.

[12] The morphology of the surface is identical to that which has not been treated with any solvents or reagents.

[13] M. T. Reetz, E. Westermann, *Angew. Chem.* **2000**, *112*, 170; *Angew. Chem. Int. Ed.* **2000**, *39*, 165; .

[14] J. G. de Vries, *Dalton Trans.* **2006**, 421.

[15] No change in the surface was observed if the Pd was exposed to the boronic ester component alone (see Figure S-1 in the Supporting Information).

[16] XPS data were also obtained in the B 1s region, but in no case was any signal detected. C 1s and O 1s spectra were also obtained but were mostly unremarkable; for the C 1s region, they showed a single peak at a binding energy of 285.0 eV. The O 1s spectra consisted of a single peak at binding energy of 532.6 eV in all cases. Both are likely due to trace contaminants on the surface as they are present in all samples.

[17] Note that the second signal observed at about 340 eV is the Pd $3d_{3/2}$ signal.

[18] M. L. Kantam, M. Roy, S. Roy, B. Sreedhar, S. S. Madhavendra, B. M. Choudary, R. L. De, *Tetrahedron* **2007**, *63*, 8002.

[19] E. H. Voogt, A. J. M. Mens, O. L. J. Gijzeman, J. W. Gues, *Surf. Sci.* **1996**, *350*, 21.

[20] P. Weightman, P. T. Andrews, *J. Phys. Chem. C* **1980**, *13*, L815.

[21] The as-received foil before extensive washing with DMF showed strong signals in the C 1s and O 1s spectra, indicative of the presence of a considerable amount of oxide and carbonaceous contaminants on the surface, in addition to a peak assignable to Pd oxide. Except for some small residual C 1s and O 1s signals, these all disappeared after the samples had been washed with DMF.

[22] It should be noted that poorly resolved XP spectra can be easily "overfit" to more peaks than the data warrant. However, if spectrum B is fit with only two peaks, the best fit is obtained with peaks of full width half maximum (FWHM) of 1.2 and 2.1 eV. This does not seem physically reasonable, as the FWHM for all other Pd spectra studied here was (1.5 ± 0.2) eV. By fitting three peaks, the FWHM values become consistent with those for other spectra observed here and also by Takasu et al., who report values of 1.6 eV: Y. Takasu, R. Unwin, B. Tesche, A. M. Bradshaw, *Surf. Sci.* **1978**, *77*, 219.

[23] L. Hilaire, P. Légaré, Y. Holle, G. Maire, *Solid State Commun.* **1979**, *32*, 157.

[24] A. Gniewek, A. Trzeciak, J. J. Ziolkowski, L. Kepinski, J. Wrzyszcz, W. Tylus, *J. Catal.* **2005**, *229*, 332.

[25] The range of binding energies observed for iodide compounds is very small, for example, the I $3d_{5/2}$ binding energies of CuI, NiI_2, AgI, ZnI_2, and CdI_2 spans a range of only 0.8 eV: S. W. Gaarenstroom, N. Winograd, *J. Chem. Phys.* **1977**, *67*, 3500.

[26] I. Pryjomska-Ray, A. Gniewek, A. M. Trzeciak, J. J. Ziolkowshi, W. Tylus, *Top. Catal.* **2006**, *40*, 173.

[27] To decrease reflection, the Pd surface needed to be coated with carbon black.

[28] *Practical Surface Analysis by Auger and X-ray Photoelectron Spectroscopy* (Hrsg.: D. Briggs, M. P. Seah), Wiley, New York, **1983**.